

## **AMENDMENTS TO THE CLAIMS**

This listing of claims will replace all prior versions, and listings, of claims in the application:

### **Listing of claims**

Claim 1. (Currently amended)      A process for production of plasmid DNA comprising:

(a)      selecting a highly productive clonal subtype of a strain of *E. coli* ~~harboring~~  
transformed with a DNA plasmid, wherein a highly productive clonal subtype comprising:

(i)      observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli*, and selecting as potentially highly productive clonal subtypes those colonies that represent a minor component of said phenotypic heterogeneity in said population of colonies;

(ii)      purifying said potentially highly productive clonal subtypes and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iii)      selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b)      cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium in a fermentation volume of greater than about 1000L.

Claim 2. (Canceled)

Claim 3. (Currently amended) [[A]] The process of claim [[2]] 1, wherein said strain of *E. coli* is DH5.

Claims 4-8. (Canceled)

Claim 9. (Currently amended) [[A]] The process of claim [[35]] 3, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

Claims 10-39. (Canceled)

Claim 40. (New) The process of claim 1, wherein said phenotypic heterogeneity is observed after the transformed *E. coli* is grown on blood agar.

Claim 41. (New) The process of claim 40, wherein the blood agar is incubated at about 30°C.

Claim 42. (New) The process of claim 41, wherein the potentially highly productive clonal subtypes that represent the minor component of said phenotypic heterogeneity are gray colored-colonies while the major component of said phenotypic heterogeneity are white-colored colonies.

Claim 43. (New) The process of claim 42, wherein the potentially highly productive clonal subtypes are purified from the blood agar.

Claim 44. (New) The process of claim 43, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined by cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

Claim 45. (New) The process of claim 44, wherein said strain of *E. coli* is DH5.

Claim 46. (New) The process of claim 45, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

Claim 47. (New) The process of claim 41, wherein the potentially highly productive clonal subtypes are purified by isolating colonies from a second type of agar that does not contain blood products, wherein said colonies correspond to the gray-colored colonies formed on the blood agar.

Claim 48. (New) The process of claim 47, wherein the plasmid copy number per cell of the purified, potentially highly productive clonal subtypes is determined by cultivating said clonal subtypes in a shake flask with feeding fermentation system using chemically defined medium.

Claim 49. (New) The process of claim 48, wherein said strain of *E. coli* is DH5.

Claim 50. (New) The process of claim 49, wherein said chemically-defined medium comprises a medium selected from the group consisting of Medium C, Medium D, Medium E, Medium F and Medium G.

Claim 51. (New) A process for production of plasmid DNA comprising:

(a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:

(i) duplicate plating the transformed *E. coli* on blood agar and a second type of agar that does not contain blood products;

(ii) observing a phenotypic heterogeneity in the population of colonies generated by the transformed *E. coli* on the blood agar, and selecting as potentially highly productive clonal subtypes those colonies that represent a minor component of said phenotypic heterogeneity in said population of colonies;

(iii) purifying said potentially highly productive clonal subtypes by isolating colonies from the second agar that correspond to those colonies that represent the minor component of the phenotypic heterogeneity in the population of colonies on the blood agar, and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iv) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium.

Claim 52. (New) The process of claim 51, wherein the blood agar is incubated at about 30°C.

Claim 53. (New) The process of claim 52, wherein the potentially highly productive clonal subtypes that represent the minor component of said phenotypic heterogeneity are gray colored-colonies while the major component of said phenotypic heterogeneity are white-colored colonies.

Claim 54. (New) The process of claim 53, wherein the *E. coli* is DH5.

Claim 55. (New) The process of claim 53, wherein said highly productive clonal subtype is cultivated in step (b) in a fermentation volume of greater than about 1000L.

Claim 56. (New) A process for production of plasmid DNA comprising:

(a) selecting a highly productive clonal subtype of a strain of *E. coli* transformed with a DNA plasmid comprising:

(i) observing a phenotypic heterogeneity in a population of colonies generated by the transformed *E. coli* when incubated on blood agar at 30°C consisting of a minor component of gray-colored colonies and a major component of white-colored colonies, and selecting as potentially highly productive clonal subtypes the gray-colored colonies;

(ii) purifying said potentially highly productive clonal subtypes, and determining the productivity of said purified, potentially highly productive clonal subtypes by measuring the plasmid copy number per cell; and,

(iii) selecting as a highly productive clonal subtype a potentially highly productive clonal subtype that exhibits a higher plasmid copy number per cell in comparison to non-selected, transformed *E. coli* clonal subtypes of the same strain; and,

(b) cultivating said highly productive clonal subtype with fed-batch fermentation in chemically-defined medium.